periprocedural intracardiac echocardiography with transesophageal echocardiography performed 6 months after transseptal puncture. We agree with Ren et al. that it is not clear whether iASD persistence accounts for adverse outcomes after MitraClip procedures or whether the persistence of an ASD just reflects adverse conditions, which lead to higher mortality and impaired functional outcomes.

The cited "discrepancies" between left ventricular end-diastolic and end-systolic volumes in patients with or without iASD were not statistically significant, and therefore, it is highly hypothetical to draw any conclusion from this finding, which might be due to play of chance in a small patient cohort. LVEF, derived from left ventricular end-diastolic and end-systolic volumes, was entered into regression analysis and failed to show significance for the prediction of 6-month mortality rates.

Most of all, the aim of our study was to assess the persistence rate of iASDs after MitraClip procedure and to report a possible influence on functional outcome. We did not aim to measure development of ASD sizes and echocardiographic flow features. We doubt the reliability of 2-dimensional echocardiography for sizing small iASDs occurring in mobile anatomical structures and echocardiography can only give us a rough estimate of the true ASD sizes. The hemodynamic consequences of ASDs should be determined with invasive measures as depicted by current guidelines (3,4).

We feel that our work contributes to a more careful evaluation of patients with persistent iASD after transseptal procedures, which might help lead to a better understanding and, in addition, to increased watchfulness regarding the clinical consequences of interatrial shunting in such patients.

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Iatrogenic Atrial Septal Defect After MitraClip Therapy

After reading the recent paper in *JACC: Cardiovascular Interventions* by Schueler et al. (1) describing the persistence of iatrogenic atrial septal defects (iASDs) after MitraClip therapy, we wish to point out an important omission. The authors stated that "persistence rates of iASDs after MitraClip procedures [are] unknown," and "this is the first study investigating the persistence rates of iASD after interventional edge-to-edge repair." In fact, our group published the first investigation on this topic in 2012, and we were surprised to see that our paper was not referenced in the paper or accompanying editorial (2). We reported on the incidence of iASD in 30 subjects undergoing MitraClip repair during the roll-in phase of the EVEREST II (Pivotal Study of a Percutaneous Mitral Valve Repair System) randomized trial, who had interpretable baseline, 30-day, and 6- and 12-month transthoracic echocardiograms (TTE). We found that iASDs were detectable in 27% of patients at 12 months by TTE. Although this is lower than the 50% prevalence of iASD detected at 6 months by Schueler et al. (1), their group used transesophageal echocardiography, which is more sensitive for iASD detection. Similar to Schueler et al. (1), we found that there was less regression in left ventricular size in patients with iASD. Importantly, we found that subjects with iASD at 12 months had more residual mitral regurgitation (MR), increased tricuspid regurgitation, and a trend toward larger LA volumes than non-iASD patients. Eighty-three percent of non-ASD patients were free from MR >2+ at 12 months versus 38% of those with iASD ($p = 0.016$). We did not note any adverse clinical events related to the presence of iASD. It is probably fair to say that the true significance of iASD remains unknown and may be related to other procedural or patient-level factors not well understood. Consideration for transcatheter closure of iASD should be

evaluated on a case-by-case basis and could be considered in patients with left-to-right shunt and evidence of progressive right ventricular or atrial enlargement, right-sided chamber dysfunction, or worsening pulmonary hypertension. Closure of iASD in patients with persistent right-to-left shunt with paradoxical embolus or arterial desaturation (hypoxemia) might also be reasonable.

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REPLY: Iatrogenic Atrial Septal Defect After MitraClip Therapy

We thank Drs. Rogers and Smith for their comments on our paper (1).

Drs. Rogers and Smith state that they were able to publish data from the roll-in phase of the EVEREST II (A Study of the Evalve Cardiovascular Valve Repair [MitraClip] System Endovascular Valve Edge-to-Edge Repair Study EVEREST II High Risk Registry) in 2012 reporting on markedly lower incidence rates of iatrogenic septal defect (iASD) after MitraClip use (27%) (2). This group reported a correlation of detectable iASD with cardiac remodeling (2), which was in part confirmed by our findings (1). Consequently, Drs. Rogers and Smith question the novelty of our data. Before we started our study program, we read their paper with great interest and acknowledge this early work. We want to point out that we did not deem ourselves to be the first group investigating incidence rates of iASD after percutaneous mitral valve repair. To the best of our knowledge we performed the first study in this field "with serial TEE examinations" (1).

Furthermore, several important differences between the 2 studies must be stressed, which makes a head-to-head comparison impossible.

First, Smith et al. (2) reported transthoracic echocardiographic findings, which has important limitations in this setting. Current guidelines define TEE the gold standard for the evaluation of interatrial shunt defects (3), and several studies were able to show significant differences in detectable iASD rates if determined with transthoracic echocardiographic findings or transesophageal echocardiography (TEE) (4). Second, the main focus of our research was to evaluate the correlation of iASD persistence with the treated patients' clinical outcomes, which was not addressed by Smith et al. (2).

Third, we included nonsurgical, highest-risk patients, including 73% of subjects with functional mitral valve regurgitation, which is in contrast to Smith et al. (2) reporting on degenerative valve disease in patients suitable for MV replacement. The persistence rate of iASD and its clinical consequences might differ relevantly between high-risk heart failure patients and the early EVEREST II population (5). As we discussed in our paper (1), we agree with Smith and Rogers that the "true" significance of iASD after percutaneous mitral valve repair remains unknown. Our results– in context with available data–showed a noticeable correlation of iASD persistence with patients' functional outcomes and survival. As we clearly stated (1), the underlying pathomechanisms for iASD persistence are not fully understood, and we emphasize the need for prospective trials addressing this topic. Currently, interventional closure of an iASD after percutaneous mitral valve repair must be planned based on a careful, individual case-by-case decision.

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